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Internal Limiting Membrane Peeling in Macular Hole Surgery; Why, When, and How?

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Internal limiting membrane peeling in macular hole surgery; Why, when and how?

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Summary statement

This review discusses the rationale for internal limiting membrane (ILM) peeling in macular hole surgery, and outlines current theories about why, how and when the ILM should be peeled, including a number of recently described variants to the basic technique.

Keywords

Internal limiting membrane; peeling; macular hole; dye; technique; inverted flap; pathophysiology; imaging; complications

Abstract

Purpose: To review the current rationale for internal limiting membrane (ILM) peeling in macular hole (MH) surgery and discuss the evidence base behind why, when and how surgeons peel the ILM.

Methods: Review of the current literature.

Results: Pars plana vitrectomy is an effective treatment for idiopathic MH and peeling of the ILM has been shown to improve closure rates and prevent postoperative reopening. However, some authors argue against ILM peeling, since it results in a number of changes in retinal structure and function and may not be necessary in all cases. Furthermore, the extent of ILM peeling optimally performed and the most favourable techniques to remove the ILM are uncertain. Several technique variations including ILM flaps, ILM scraping and foveal sparing ILM peeling have been described as alternatives to conventional peeling in specific clinical scenarios.

Conclusion: ILM peeling improves MH closure rates but can have several consequences on retinal structure and function. Adjuvants to aid peeling, instrumentation, technique and experience may all alter the outcome. Hole size and other variables are important in assessing the requirement for peeling and potentially its extent. A variety of evolving alternatives to conventional peeling may improve outcomes and need further study.

Introduction

"Idiopathic" full thickness macular hole (FTMH) is a vitreomacular interface disorder, which can lead to severe visual impairment.[1] It is estimated that it is present in 33 of every 10000 individuals over the age of 55 years, while the incidence has been reported to be 4-8.7/100000 per year, with female-to-male ratio to be 2-3:1.[2,3] Gass classified MHs into 4 stages based on careful fundoscopy; in stage I a central yellow spot is observed at the foveal centre, with loss of the foveal depression (stage Ia), which can be followed by the formation of a ring shaped yellow reflex (stage Ib) without a full thickness defect. In stage II, a small FTMH (<400 μm) is formed, usually with a visible operculum. In stage III, the FTMH widens to more than 400 μm in diameter, but complete posterior vitreous detachment (PVD) has not yet occurred, whereas stage IV is the same as stage III after complete vitreous separation from the disc.[4] In 2013 the International Vitreomacular Traction Study Group proposed an anatomical classification of vitreoretinal interface disorders using spectral domain optical coherence tomography (SD-OCT) and defined FTMH as "interruption of all retinal layers extending from internal limiting membrane (ILM) to the retinal pigment epithelium (RPE)", hence classifying precursor Gass stage I lesions as vitreomacular traction (VMT).[5] They also sub-classified MHs based on their size as small (<250 μm), medium (250-400 μm) and large (>400 μm), and based on the presence or absence of VMT.[5]

The pathogenesis of "idiopathic" FTMH is not completely understood, but is thought to involve anteroposterior traction and/or tangential traction exerted by the posterior vitreous cortex at the fovea from an incomplete PVD as a result of ageing. Specifically, tractional forces on an abnormally persistent vitreofoveal attachment, after perifoveal vitreous separation may result in anteroposterior traction,[6-8] while tangential traction may derive from contraction of the residual vitreous, which remains over the fovea after PVD as well as from invasion and proliferation of Muller cells over the ILM.[4] Tangential traction has a significant role on its own after the formation of FTMH with transmission of inner retinal forces to the photoreceptors via Muller cells and enlargement of the hole.[9] Additionally, and as proposed initially by Tornambe, once there is a break in the inner retina this results in destabilization of the foveola with progressive retinal hydration, enlargement of the hole and elevation of the outer retina from the RPE with a cuff of subretinal fluid.[10,11] Despite the fact that the majority of FTMHs are

classified as "idiopathic" and related to ageing, they may also be associated with high myopia, ocular trauma, as well as with, or following retinal detachment.[6,12]

Until the early 1990s, there was no treatment for established FTMH. During the evolution of vitreofoveal separation, VMT resolves in approximately 30% of cases[13]; however, spontaneous FTMH closure is less common occurring in approximately 5-10% of mainly early cases.[14-17] The rationale for surgical intervention originated in the identification of centrifugal traction as the cause of MH formation, rather than permanent loss of foveal tissue being responsible for the visual deterioration.[18] The first article reporting the results of vitrectomy for FTMH treatment was published in 1991,[19] and the first report of ILM peeling specifically for MH in 1997 by Eckardt et al.[20] Surgery for FTMH is now one of the commonest vitreoretinal surgeries undertaken accounting for about 10% of all vitrectomies in the United Kingdom.[21]

ILM peeling has gained widespread acceptance, since it has been shown to improve closure rates and prevent late postoperative reopening, one of the most common complications of successfully closed MH.[20,22,23] However, some authors argue against ILM peeling, since it may cause iatrogenic damage, result in a number of changes in retinal structure and visual function, and may not be necessary in all cases. The extent of ILM peeled during surgery, the technique of ILM peeling, and several variants of how the ILM is peeled have been described. Surgeons are thus faced with a number of options when approaching these cases. These choices are now reviewed and put into context.

ILM structure

The ILM forms the inner boundary of the retina and is considered the basement membrane of the Muller cells, but is at least partly formed from proteins shed into the vitreous cavity during embryogenesis from the lens and ciliary body.[24] It is composed of collagen types IV (>50% of total ILM protein) and VI and a wide variety of proteoglycans including the heparan sulphate proteoglycans Perlecan, Agrin, and Collagen-XVIII as well as Nidogen and Laminin 111,[25] many of which are involved in both the adhesion of the ILM to the retina but also the adhesion of the cortical vitreous to the ILM. The ILM thickens and becomes more rigid with age with a relative increase in the concentrations of Collagen IV

and Agrin and a reduction in Laminin.[26] Its thickness varies across the fovea reaching its maximum thickness at a point approximately 1000 microns from the foveal centre, being very thin at the foveal centre (~0.150 microns) and then gradually thinning again towards the periphery.[27] Its vitreous side is smooth where it meets the condensed cortical vitreous, but is deeply convoluted on the retinal side (Figure 1).[27] Although thin, its mechanical strength is in the megapascal range similar to articular cartilage and about a 1000-fold stronger than cell layers, forming at least 50% of the retinal rigidity.[28,29] Its removal thus reduces retinal compliance and being anchored at the optic disc, after peeling there is a movement of the temporal retina towards the disc.[30,31] Interestingly the ILM has approximately 5 times greater rigidity on its retinal side compared to its vitreous side, accounting for its tendency to scroll inward when peeled, and perhaps adding to tangential inner retinal traction in a centrifugal direction.[27]

Rationale for peeling the ILM in MH surgery

ILM peeling is thought to improve FTMH closure by a variety of mechanisms. As discussed above, despite the ILM being only few microns thick, it contributes very significantly to retinal rigidity and its removal results in an increase in retinal compliance, aiding hole closure.[29] When vitreous separation occurs from the retinal surface, either spontaneously or surgically created, remnants remain on the ILM surface particularly at radii of 250 and 750 microns.[32,33] The ILM has also been shown to form a scaffold for the proliferation of cellular components such as myofibroblasts, fibrocytes and RPE cells, while glial cells may also migrate onto the surface of the ILM, creating a tangential contractile force. Surgical peeling of ILM therefore not only removes the remaining macular cortical vitreous which could exert residual tangential traction, but also inhibits the formation of postoperative epiretinal membranes and secondary tangential traction.[7,29,34] Finally, ILM removal, with its trauma to the Muller cell end feet, may lead to a retinal glial cell proliferation response, which could paradoxically enhance MH contraction and repair.[7,29,34]

Effects of ILM peeling

1) **Macular hole closure**

Several randomized studies (RCT) have been carried out on the efficacy of ILM peeling in IMH surgery. In one large RCT, closure was achieved in 84% of the patients undergoing ILM peeling compared to 48% who did not undergo ILM peeling (P<0.001) at 1 month postoperatively.[35] A recent Cochrane review of four RCTs concluded that the available evidence supported ILM peeling in Stages 2, 3, and 4 IMHs.[23] However, it should be noted that some of these studies were without OCT measurements of the hole size, and the evidence base for peeling small sized FTMHs is less robust, where the closure rate without ILM peeling can be high.[36]

Late hole re-opening

A recent meta-analysis of 5,480 FTMH surgeries among 50 publications has shown a significantly lower rate of FTMH reopening after ILM peeling than in surgery without ILM peeling.[22] Specifically, the reopening rate without ILM peeling was 7.12% compared with 1.18% with ILM peeling (odds ratio: 0.16; 95% confidence interval: 0.11-0.22, p<0.0001).[22]

2) Retinal consequences of ILM peeling

ILM peeling is a challenging surgical procedure and has a number of potential detrimental consequences not least of which relate to the surgeon learning curve.

a) Immediate

Focal retinal hemorrhages, nerve fiber layer damage and full thickness retinal defects can be caused by instrument trauma at the initiation and ILM pick up points, whilst iatrogenic eccentric holes have been also reported.[37-39] It is also observed that as the ILM is peeled, and discrete from instrument trauma, superficial retinal hemorrhages occur as the ILM is avulsed from the retinal surface. These are commonest nasally and thought to represent traction on Muller cells which surround capillaries within the superficial retinal layers (Figure 2).[40]

b) Inner retinal changes observed on retinal imaging

Swelling of the arcuate retinal nerve fibre layer (SANFL) on SD-OCT seems to be the earliest short-term anatomic change in the macula after ILM peeling. Clark et al described SANFL as

hyperautofluorescent arcuate striae in the macular region, with a corresponding swelling on SD-OCT. The sign disappeared in all patients after a mean period of 2 months and did not cause any effect on visual acuity.[41] SANFL may be attributed to direct surgical trauma caused by forceps at the time of ILM grasping prior to peeling or may represent subclinical trauma of the inner retina due to Muller cell endplate damage.[42]

A 'Dissociated Optic Nerve Fibre Layer' (DONFL) appearance, first reported by Tadayoni et al after ERM and ILM peeling, occurs a few months after ILM peeling in macular hole surgery and is thought to relate to loss of distal Muller cell processes resulting in dimpling of the nerve fibre layer possibly secondary to their disaggregation.[43-45] Indeed, its extent has been correlated with the amount of Muller cell debris on the peeled ILM on electron microscopy and could be regarded as a marker for the depth of the plane of ILM separation (Figure 3). The appearance is mostly easily seen on blue reflectance imaging and near universally after ILM peeling on en face OCT (Figure 4). It is unclear if it has functional consequences, with some authors reporting defects in microperimetry and reduced macular sensitivity linked to the areas most affected by DONFL.[40,43,44]

A transient increase in RNFL thickness in the area of peeled ILM may occur postoperatively. This can progress to RNFL thinning potentially due to focal damage to the inner retinal layers[46,47] especially on the temporal side of the fovea which appears to be an area more vulnerable to the effects of peeling.[48,49] Nevertheless, it is unclear whether these findings are purely secondary to the ILM peeling or other factors, such as dye toxicity and air-infusion stress related to MH surgery.

c) **Changes in retinal morphology**

A variety of morphologic changes in the retina have been noted after ILM peeling, including a movement of the fovea toward the optic nerve head, which has been associated with thickening of the nasal retina and thinning of the temporal retina.[30,50] The retinal movement is centripetal but with greater movement in the horizontal meridian than vertical, and greater movement of the temporal retina toward the disc than nasal.[50,51] The observed retinal displacement has been related to the extent of postoperative metamorphopsia and also the postoperative appearance of a DONFL.[51,52]

d) Functional consequences

Some authors have observed paracentral scotomas and reduced central retinal sensitivity after ILM peeling whilst other authors have found no functional consequences possibly relating to the relating to difficulty of testing.[44,53,54] Al-Abdulla et al found a statistically significant VA improvement of at least 3 lines at 3 months in 79.2% of 24 eyes with FTMH who had ERM removal only compared with 44.8% of 29 eyes with additive ILM removal.[55] Pilli et al found an association between the reduced inner retinal volume in the macular after ILM peeling and postoperative visual outcome suggesting a detrimental effect of peeling on function.[56] Despite this and importantly there was no difference observed in visual acuity outcomes in the RCTs on ILM peeling. However, these were analysed on an intention to treat basis and did not take into account the anatomical status and requirement for repeat surgery at the time of the designated endpoints (i.e. the macular holes without primary ILM peeling underwent redo surgery with peeling prior to the designated endpoint).

One way of addressing this is to look only at patients with primary hole closure with peeling and without peeling in randomised controlled studies. Christensen et al in their RCT of FTMH found that there was a trend towards better mean BCVA in the non-peeling group of stage 2 macular holes (78.2 letters) as compared with the peeling group (70.9 letters, p=0.06) although there was no suggestion of a difference in stage 3 holes, and it is uncertain if the dye used (ICG) had any effect on visual outcome.[57] Furthermore, in those patients who required a second surgery with ILM peeling after non-closure without peeling, there was a significant reduction in functional outcome indicating that primary closure is optimum. It should be also noted that there may be more subtle visual effects caused by ILM peeling, which have not been systematically or reliably measured (e.g. low luminance vision and contrast sensitivity).

e) Electrophysiological changes

Terasaki et al described the electrophysiological changes in a cohort of patients with FTMH undergoing surgery with and without ILM peeling. There was a selective delay in the extent of recovery of the focal macular electroretinogram (ERG) b-wave 6 months after surgery in the ILM peeling group indicating a change in inner retinal function in the ILM peeled area.[58] The same group also noted a reduction of the

amplitude of the photopic negative response of the photopic ERG after surgery ($P < 0.05$), suggesting altered ganglion cell function although other groups have found no changes in multifocal ERGs and Oscillatory Potentials after ILM peeling MH surgery.[59,60]

Is ILM peeling always required to close a macular hole surgically?

Specific types of FTMHs have well established lower closure rates with surgery. Large (>400 μm), chronic (>6-12 months) and traumatic FTMH have lower rates of closure[34] and most authors would always peel the ILM in these cases. Similarly, FTMH associated with high myopia especially those associated with posterior pole staphyloma, myopic retinoschisis and localized retinal detachment benefit from ILM peeling.[61] Increasingly surgeons are opting to perform ILM peeling with ILM flap creation in these cases.

For smaller MHs especially those less than 250 microns the need for ILM peeling is more controversial. Notably, Tadayoni et al have found that ILM peeling seemed not to be useful for MH less than 400 μm in diameter.[36] It is important to observe however that in this study face down positioning and long acting gas were used, both of which conceivably would alter the requirement for ILM peeling. It is also well recognized that spontaneous hole closure with VMA release is much commoner in small holes than larger ones and the same relationship is also seen with expansile gas and Ocriplasmin induced hole closure, both in whom the ILM is intact. Smaller holes most likely have lower degrees of tangential traction and studies have indeed shown that the extent of ILM vitreous side debris (residual vitreous and ERM), assessed by both electron microscopy and ILM specific dye staining appearances, is related to hole size and stage. Stage 4 holes regardless of hole size were associated with larger amounts of ILM surface debris.[62] Another factor to be taken into consideration is hole shape. Holes with a small difference between the mid-point diameter and base diameter i.e. more rectangular-shaped as opposed to triangular shaped holes have a higher rate of closure after treatment with Ocriplasmin, perhaps relating to their early stage of evolution (Figure 5).[63] It could be postulated that the same finding would apply to spontaneous and surgical closure. Thus small rectangular shaped holes, especially those with VMT and with an even dye staining pattern suggestive of no or limited vitreous side material on the ILM might be considered be the optimum candidates for vitrectomy without ILM peeling.[10,62,]

ILM peeling techniques

ILM is thin and translucent and closely adherent to the retinal nerve fibre layer. There are several surgical techniques, adjuvants and equipment developments which have been devised to identify the ILM and allow it to be peeled without collateral retinal damage.

a) Visualizing the ILM

Staining of the ILM with an adjuvant significantly improves the effectiveness and efficiency of the procedure.[64-66] Available agents are either dyes which stain the ILM, including indocyanine green (ICG), trypan blue and brilliant blue, or coatings such as triamcinolone acetonide crystals (TA).

The first dye described was dilute ICG which was found to offer a good contrast between stained and unstained retina.[67] However shortly after the first report there were reports of adverse effects in patients who had undergone ICG-assisted surgery.[68,69] Studies went on to show highly dose dependent toxicity in a variety of in vitro models[70-72] with clearly damaging inner retina changes in combination with intraoperative light exposure,[73] as well as optic nerve damage,[74] symptomatic visual field defects and poor visual acuity outcomes.[75] The concentration of ICG used is critical, as is the application time and light exposure, since ICG has known photosensitizing properties and its resultant decomposition products after illumination lead to inner retinal toxic reactions and larger amount of retinal side ILM cellular debris after peeling. Therefore, if used at all ICG should be used in a low concentration with the minimum exposure time and light levels.

Based on the concerns about the use of ICG, other vitals dyes including trypan blue and brilliant blue G (BBG) were subsequently developed for ILM peeling. Trypan blue is not specific for ILM and stains ERM as well but is less toxic than ICG.[76] Brilliant blue G has been found to be safe in routine clinical practice, showing selective ILM staining similar, albeit with lower contrast to ICG.[62,77] Heavier than water dyes formed by mixing trypan blue and/or BBG with either deuterium or polyethylene glycol have enhanced ease of use whilst maintaining the degree of contrast obtained.[78]

Dyes have the interesting effect of increasing retinal rigidity which is illumination dependent to some extent. Increased ILM rigidity facilitates peeling and the initial creation of an ILM flap although

potentially increasing rigidity may alter the ILM cleavage plane from the retina with a deeper plane of separation.[79,80]

Regardless of which dye is used, dye concentration and contact time (i.e. the time that the dye is left on the retinal surface before being aspirated off) should be minimized and contact times of 5-10 seconds can give adequate staining contrast.[62] Light exposure and peeling times are also factors which could influence the occurrence of observed toxicity. Indeed, recently another dye acid violet 17 was reported to successfully stain the ILM resulting in less retinal debris but with lowered staining contrast than brilliant blue.[81] No toxicity was reported but subsequent reports have, possibly relating to differences in usage, and the product has now been withdrawn from the market.[81,82] Clear guidance on toxicity testing and clinical application before market authorization are clearly needed. Recent developments in digital viewing using selected wavelengths and safer endoilluminators may further reduce effective dye concentrations for surgically acceptable contrast.[83]

b) ILM peel initiation

A critical step in ILM peeling is the creation of an ILM flap to allow the peel to be initiated. A variety of instruments have been used to do this including picks and micro-vitreoretinal (MVR) blades. A flap can also be created using a gentle sweep of a diamond dusted membrane scraper (DDMS) across the ILM surface and recently a micro-serrated nitinol loop (Finesse Flex Loop, Alcon) of variable length, and hence stiffness, has been introduced for the same purpose. Many surgeons use a direct 'pinch' technique using custom designed forceps to initiate a flap. The ILM alone is grasped in forceps, lifted very slightly form the retinal surface and then pulled tangentially creating a flap with the rip point 180 degrees from the direction of pull. Forceps design and hand control are critical to avoid accompanying retinal tissue in the initial 'pinch'. The optimum point of peel initiation is uncertain. The ILM is thickest approximately 1000 microns for the foveal centre and coincides with the point of maximum ILM rigidity. The temporal retina is thinnest and the nasal retina carries the papillo-macular nerve fibre bundle, and therefore a point on the retina 1000 microns above or below the foveola may be optimum (Figure 6).

c) ILM peel propagation

Once the flap is created, vitreoretinal forceps are most commonly used to remove the desired area of ILM using circular movements around the fovea, similar to capsulorrhexis in cataract surgery.[84] The optimum angle of peeling is uncertain but computer modelling using parameters from ERMs has suggested that peeling at 150 degrees to the retinal plane (i.e. acutely angled in the direction of peel) is optimum in terms of retinal stress.[85] Studies using intraoperative OCT may also yield important information on guiding surgeons in this regard.[86]

Some surgeons use a DDMS to both initiate and complete peeling.[87] It is worthy to note that a difference in the degree of a DONFL appearance after ILM peeling using a forceps technique compared to that using a DDMS technique to initiate and complete the peeling has been observed, with less DONFL and retinal debris on TEM with forceps peeling.[87]

d) ILM peeling size

There are currently no prescribed parameters for the optimum extent of ILM to be peeled during surgery for macular holes. Most surgeons aim to peel an approximately one disc diameter radius of ILM around the foveal centre but reports vary hugely from 0.5 disc diameters to 3 or more.[88] Enlarging the ILM peel area can result in hole closure in failed cases undergoing revision surgery, and some authors have argued for large ILM PAs in all cases.[89] However, it is not at all clear what the optimum ILM peel size should be in any particular case.

It has been observed that the extent of the area of ILM removed is strongly associated with the degree of a number of postoperative changes including shortening of the disc fovea distance, the extent of a DONFL appearance observed and importantly the postoperative visual acuity.[30]

Modi et al carried out a prospective study of 50 patients undergoing surgery with ILM peel radii of 1 and 1.5 DDs.[90] They found no significant difference in hole closure rates but better visual results in the smaller peel radii group with less retinal nerve fibre layer thinning particularly temporally.

Conversely, Bae et al carried out a randomized controlled study of 65 eyes with ILM peeling radii of 0.75 and 1.5 DDs.[91] They found no difference in visual outcomes but did find a benefit of larger peels with regard to an improvement in metamorphopsia.

Currently, it is thus unclear as to the extent of ILM that should be optimally peeled during surgery for macular holes. Hypothetically, there may be a minimum ILM peel area for a set size of macular hole to allow enough reduced retinal compliance to permit closure. This area may vary with hole chronicity and other factors. Larger ILM peels would ensure that this threshold was passed but at the expense of greater inner retinal changes and potentially reduced visual function.

Variants of ILM peeling techniques

A) Techniques to improve closure or treat non-closure

Inverted ILM flap technique

The prognosis of idiopathic macular holes depends mainly on the duration, stage and diameter of the hole with large chronic stage 4 holes having relatively low closure rates.[34] Myopia is also a well-known risk factor for non-closure.[92]

The inverted ILM flap technique was introduced by Michalewska et al in 2010 for the treatment of large stage 4 MHs,[93] but has subsequently been extended for MHs related to high myopia with and without associated peri-foveal retinal detachment.[94] The technique as initially described involved circumferential ILM peeling but leaving a frill of ILM around the hole, loosely attached to the edge of the hole rim. This is typically trimmed to shorten the length of the frill to ~0.5-1mm in length, and then inverted into the hole using forceps.[94] A zero vacuum trimming technique lessens the risk of inadvertent ILM flap avulsion.[95] Several publications have strongly suggested that the ILM flap technique improves closure in these difficult to close scenarios. Several variations of the technique have been proposed to reduce the requirement for posturing, surgical time and risk of retinal trauma including just creating a flap on one side of the hole only and folding it over as a flat sheet over the hole. However recent reports suggest that manoeuvers other than the creation of the flaps themselves (e.g. trimming of flaps) do not improve success rates, although the original inverted ILM flap technique may offer advantages over the single sheet variant technique in large holes.[96-105]

The technique is thought to work by both a scaffold effect and the presence of Muller cell fragments on the peeled ILM acting to stimulate a glial cell response aiding closure.[93] Although closure rates are improved, the question arises as to whether visual prognosis is affected in any way by the

presence of the non-neural retinal sheet in the hole. Imai and Azumi reported a case of expansion of submacular RPE atrophy after an otherwise successful inverted ILM flap for a persisting large stage 4 macular hole, which was previously treated with PPV without ILM peeling and remained open. It was uncertain whether this was related to dye toxicity or to the potential secretion of inflammatory cytokines from the vitreous, inducing Muller cell activation, followed by both RPE atrophy and gliosis.[106]

ILM free flap

A related technique is the use of an ILM free flap in patients who have a persistent MH hole after previous surgery using ILM peeling**.** During redo surgery, a free patch of peripheral peeled ILM is placed over or in the FTMH. There are many uncertainties as to the optimum way to do this.[107] Some surgeons fill the hole with ILM, sometimes using viscoelastic substances or blood as a 'glue' to hold the ILM in place whilst others attempt to place the ILM as a single sheet across the hole. Heavy liquids can be used to hold the flap in place during a fluid air exchange before gas exchange and face down positioning for a few days.[108-114]

B) Techniques to reduce ILM peeling

Foveal sparing ILM peeling

An interesting idea to reduce the damage from ILM peeling around the hole is the foveal sparing ILM peeling.[115] In this technique, the ILM is peeled off other than a central ring extending ~ 400 microns around the MH rim using a combined peeling approach with forceps and scissors if needed.[115] The flap can also be trimmed down in the same way as the ILM flap technique, the difference being that the zone where the ILM is left attached to the retina is broader (Figure 7). It was postulated that by preserving the ILM centrally, foveal microstructure would be better preserved. Ho and colleagues presented a retrospective series of 28 eyes with small macular holes and VMA, 14 of which had foveal sparing ILM peeling done. All eyes had a closed hole following surgery, but in the foveal sparing group visual acuity, ellipsoid zone and ELM restoration, and reformation of a smooth foveal umbo were significantly better.[115] It was postulated that this restoration of the central umbo would aid the normal optical light fiber's role of Muller cells.[116]

ILM abrasion technique

An alternative to ILM peeling that has been proposed is ILM abrasion, aiming not only to remove all ILM surface vitreous and ERM material, but also potentially to thin the ILM and loosen its adhesion to the underlying retina whilst still stimulating glial cell activation. In the technique as described by Mahajan et al, after performing the core vitrectomy, a DDMS was gently brushed convex side down over the macula in both circumferential and radial motions in an area of 1 disc diameter surrounding the MH taking care to avoid inadvertent ILM tears.[117]

Mahajan et al using the above technique in 100 eyes with stage 2-4 holes reported a 94% closure rate with a single procedure; a proportion which is comparable with that of published rates where ILM peeling was performed conventionally.[117,118] Visual results were similarly comparable. There was no difference in the closure rates between any of the stage categories. Triamcinolone was used as a stain avoiding any potentially dye toxicity. It is a new technique and clearly needs further study especially of longer term reopening rates, however it also suggests there may be other alternatives to traditional 'peel and remove' ILM techniques that could be evaluated.[119]

Conclusions

ILM peeling has now become an engrained part of macular hole surgery so that most surgeons peel all holes. However even the most perfectly performed ILM peel has consequences on retinal structure and function which may be detrimental in some patients. The specific technique of ILM peeling used, who peels the ILM and any dye used may add to the risks. In some holes there is no doubt that peeling is indicated; large, chronic, myopic and traumatic MHs especially. Inverted ILM flap surgery may have an expanding role in some of these cases. Small and recent onset macular holes may not however require ILM peeling in all cases, and both small and medium sized macular holes may benefit from an evolving number of alternative ILM peeling options. None of these options have been evaluated in RCTs and further study is needed.

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Figure legends

Figure 1: Transmission electron microscopy image of perifoveal retina in a 6-year-old Macaque monkey showing complex relationship between internal limiting membrane (ILM), Muller cells and nerve fibre layer fascicles. Asterix: ILM, Long arrow: Muller cell, Black cross: nerve fibre fascicle. Scale bar 2 microns.

Figure 2: Transmission electron microscopy image of inner retina perifoveal retina in a 6-year-old Macaque showing a capillary within the nerve fibre layer. Long arrow: ILM, Short arrows: Muller cells, Block arrow: blood vessel with surrounding Muller cell. Scale bar 10 microns.

Figure 3: Transmission electron microscopy of a human peeled ILM sheet. Black arrows: remnants of Muller cell end feet on retinal side of ILM after peeling - larger fragments of specimen on right. Scale bars 2 microns.

Figure 4: Upper left image shows a blue reflectance image of a closed macular hole after ILM peeling. The area of peel is outlined by a white dotted line. Note DONFL appearance within the peeled area. Lower left image shows corresponding 'en face' spectral domain-optical coherence tomography (SDOCT) image with dimples evident in nerve fibre layer corresponding to the DONFL appearances. Upper and lower right showing horizontal SDOCT line scan images: Upper image corresponding to black dotted line and lower to white dotted line on en face image.

Figure 5: Examples of horizontal SDOCT images of macular holes. The upper images show rectangular shaped macular holes with a small difference between the base diameter and minimum linear diameter ('narrow width factor'), and lower images show macular holes with a more triangular configuration with a larger difference ('wide width factor').

Figure 6: The ILM is thickest at a point approximately 1000 microns from the foveal centre shown as a dotted line. Peeling is most optimally initiated from this area above or below the fovea and peeled concentrically.

Figure 7: Intraoperative images during ILM peeling using BBG dye. Left image shows a frill of ILM around the rim of a macular hole with the vitrectomy cutter being used with zero vacuum to trim the edge of the ILM. The right image shows a completed peel using a foveal sparing technique with a narrow rim of adherent ILM left around the hole.

Figure 1

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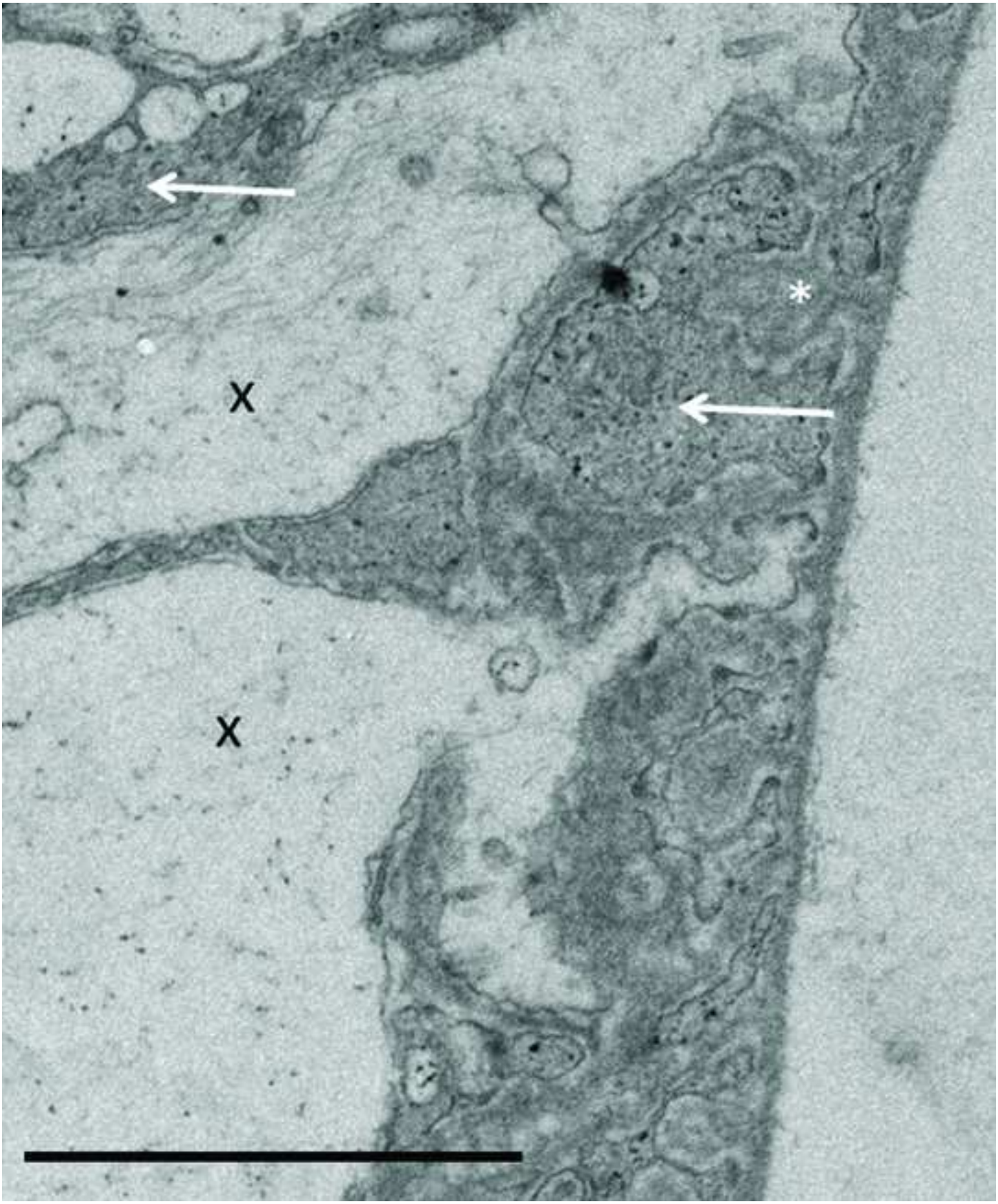

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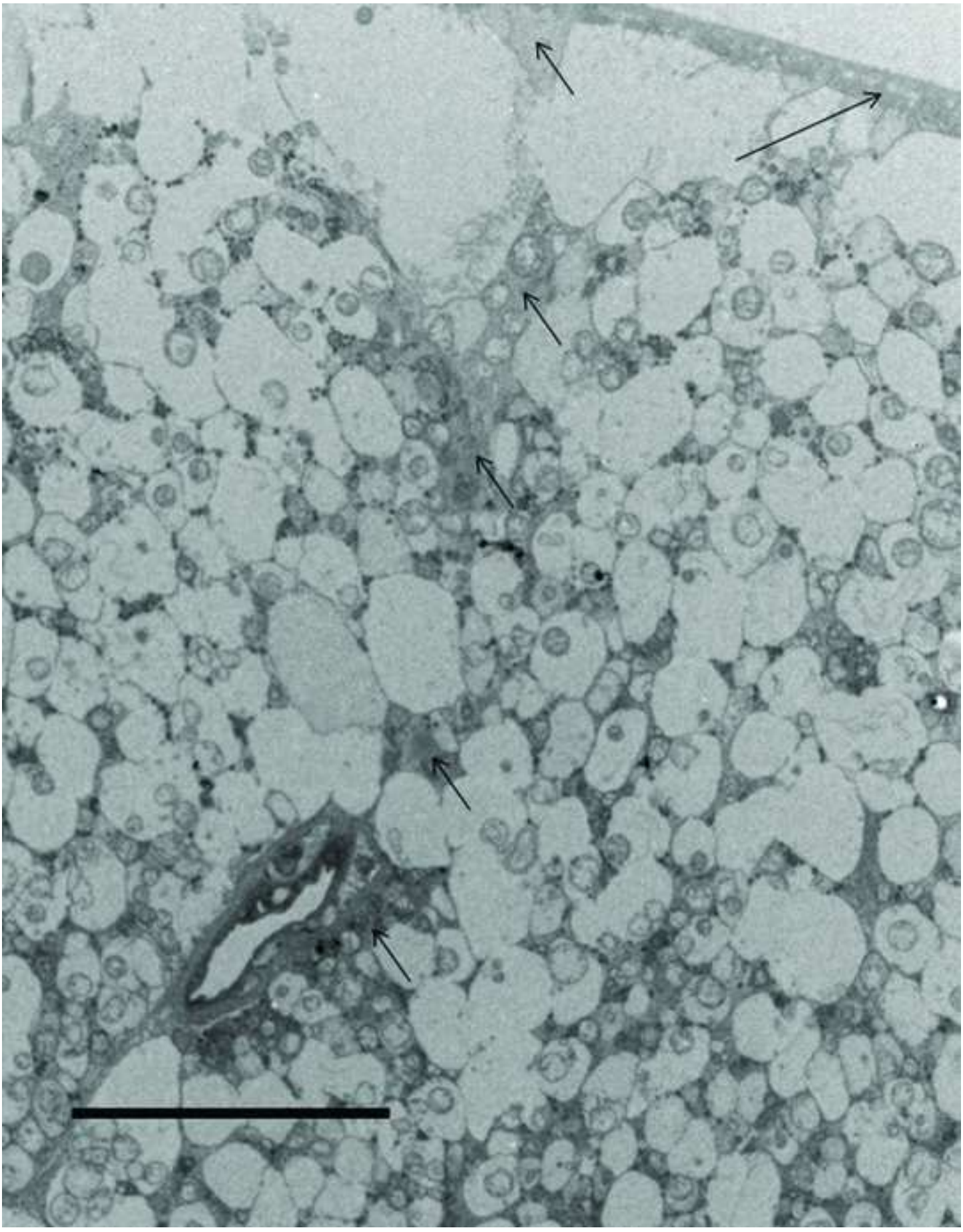

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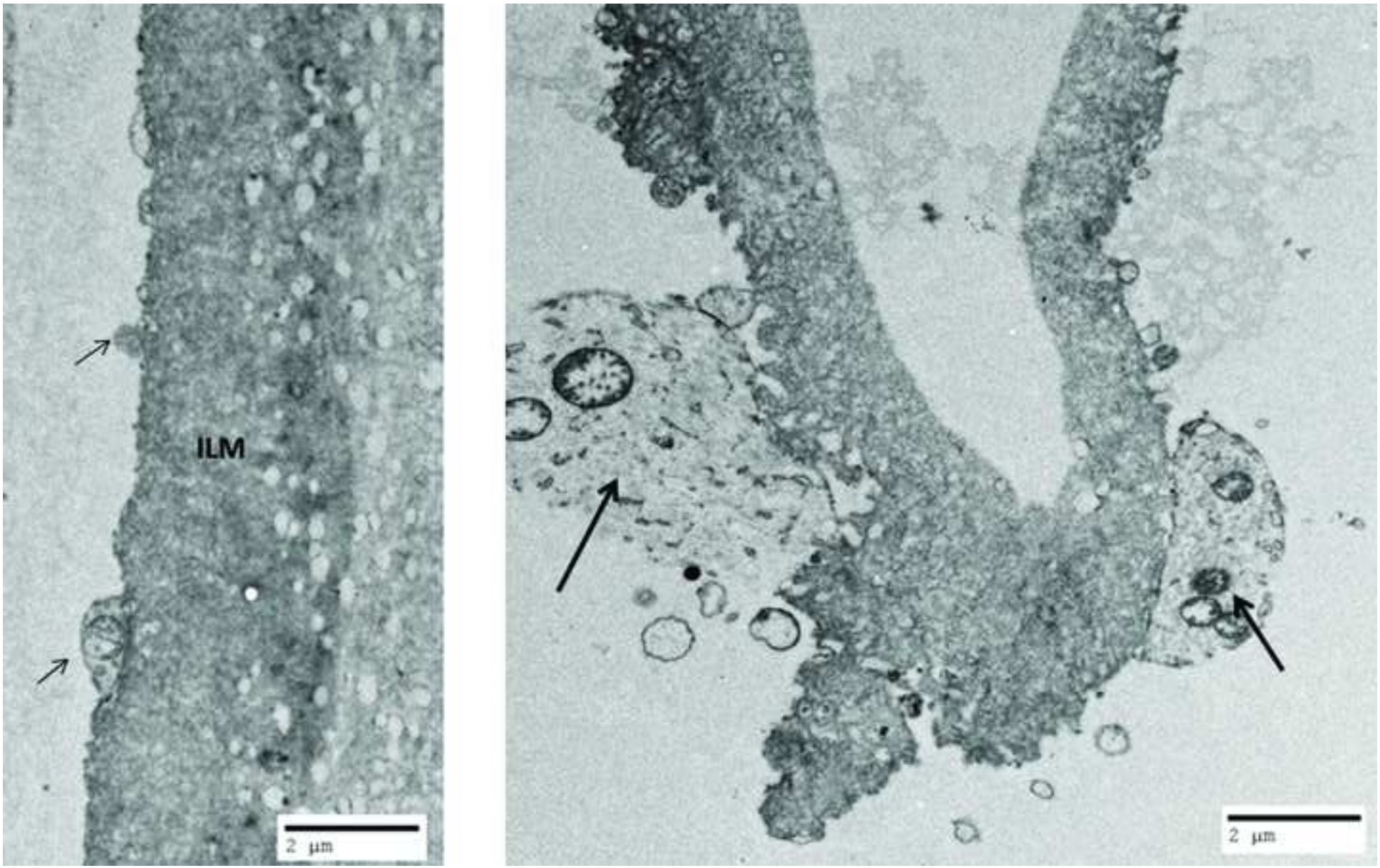

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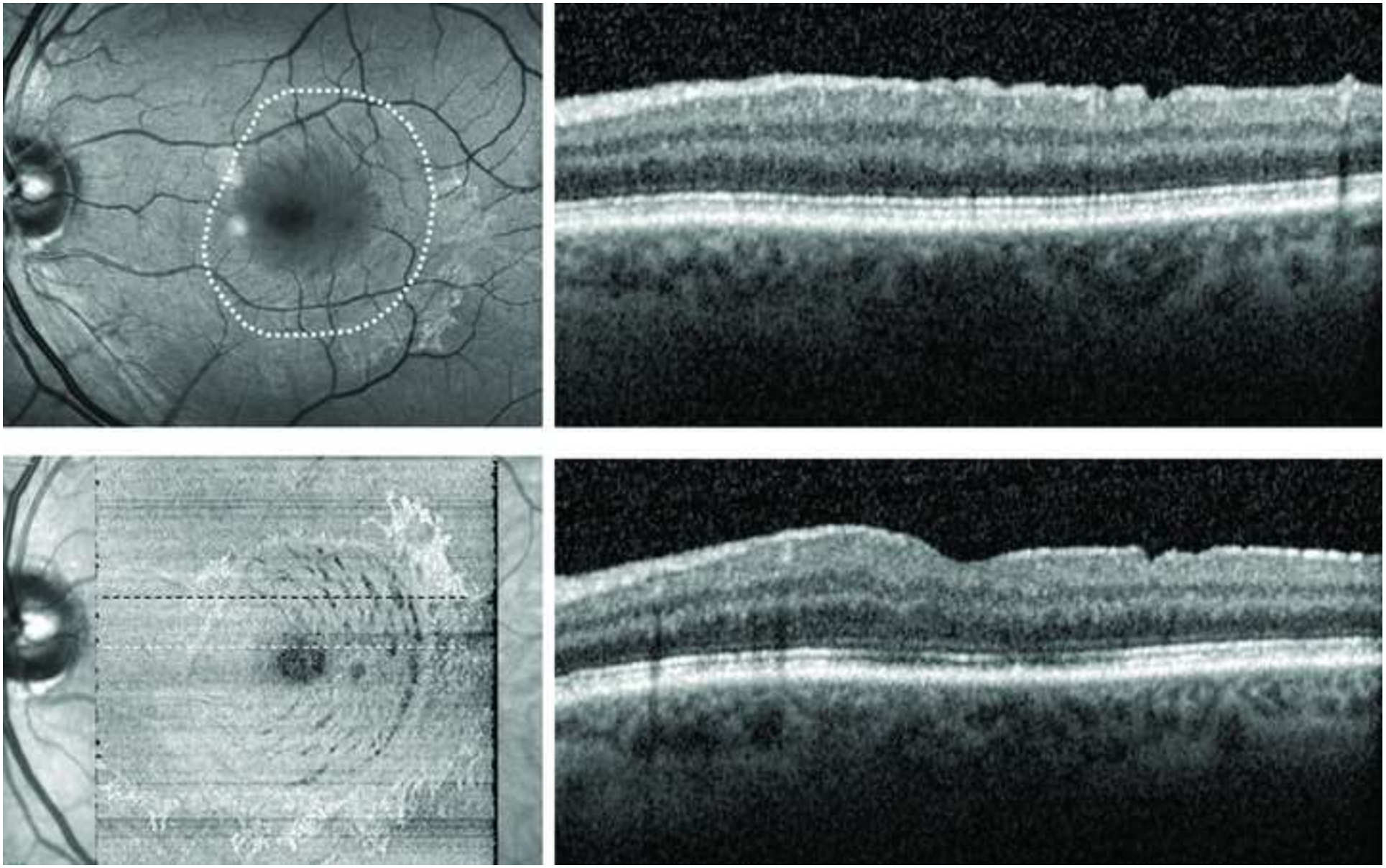

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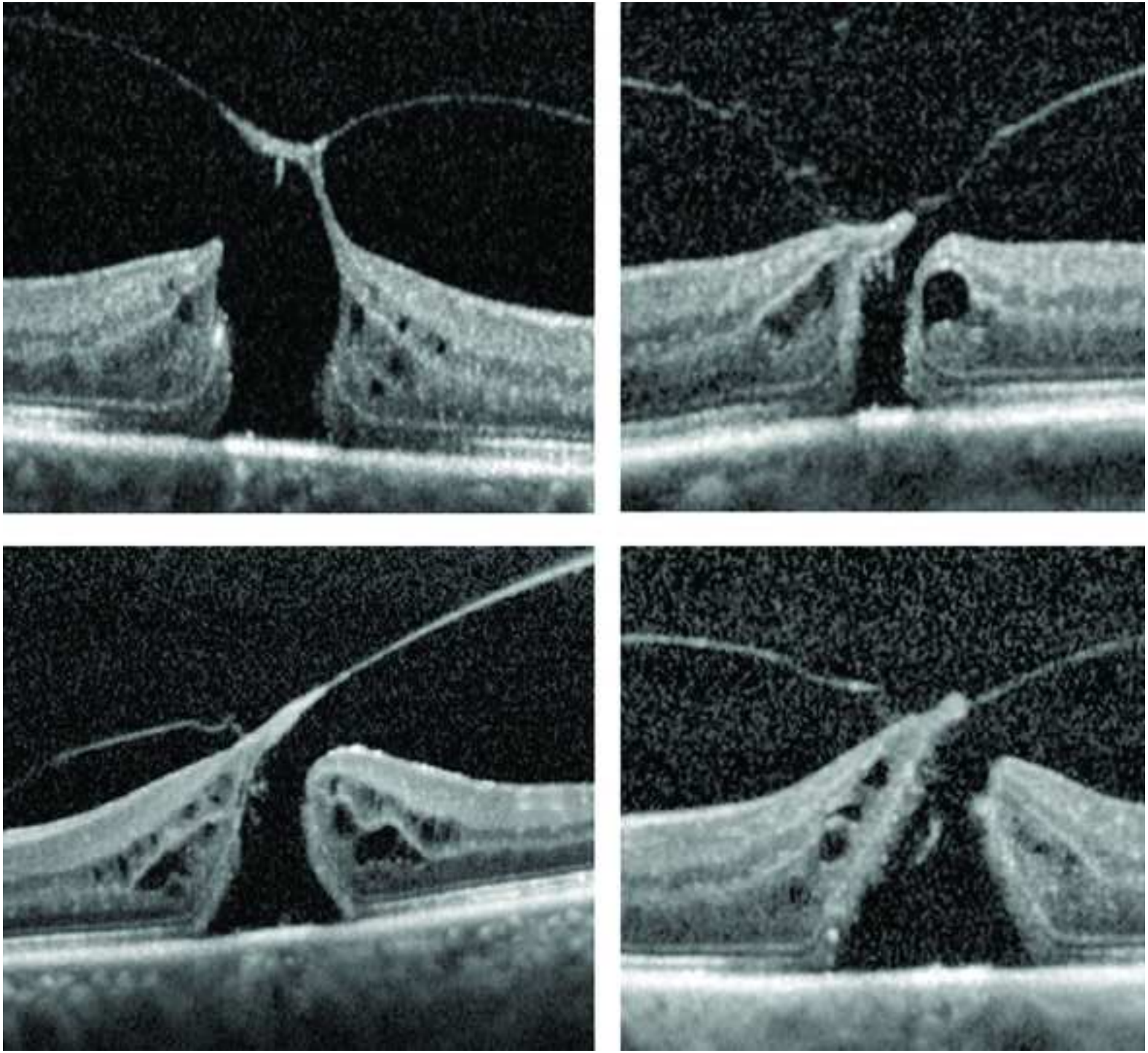

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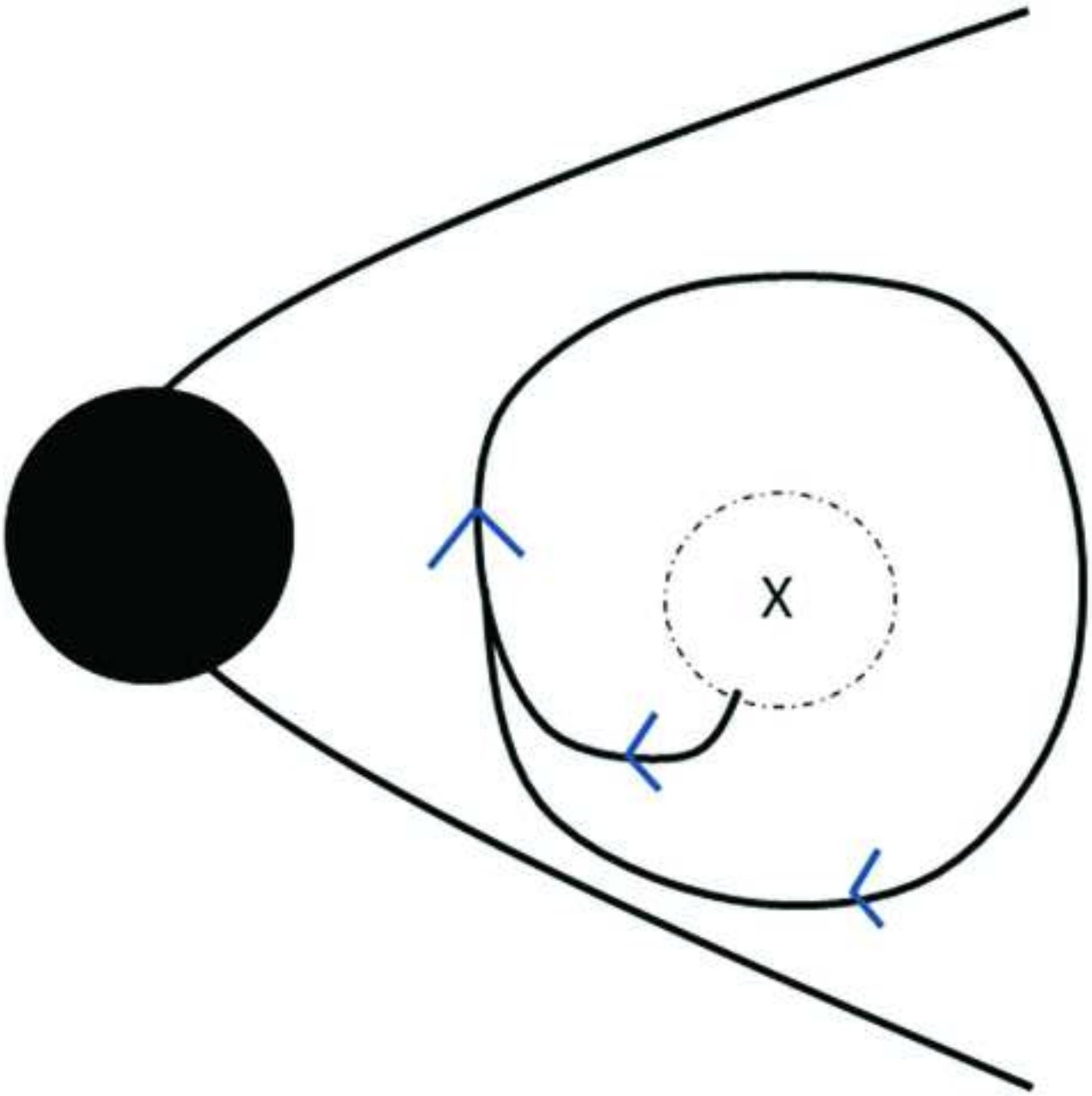

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